REMARKS

Claims 4 to 8, 24, and 26-43 are now in the case.

Claims 4, and 24, have been amended. Claims 5 to 8 and 26 to 39 remain unchanged. Claims 40-43 are new and simply relate to a host cell comprising the recombinant vector of claims 5, 26, 32 and 36, respectively. Claim 25 has been cancelled.

Applicant acknowledges with thanks the allowance of claims 30-39.

Reconsideration of this Application and entry of the foregoing amendments are requested. Claims 4, and 24 have been amended in view of the Office Action, to better define what the Applicant consider his invention and to put the application in condition for allowance.

REJECTIONS UNDER 35 U.S.C. § 112 FIRST AND SECOND PARAGRAPHS

The Examiner has rejected claims 4 and 24 under 35 U.S.C. § 112, **first** paragraph. The Examiner alleges that the specification does not reasonably provide enablement for a nucleic acid encoding proteins that have at least 95% identity to an isolated nucleic acid encoding the amino acid sequence encoding SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:2, SEQ ID NO:4; amino acid residues 1-577 and 2-577 of SEQ ID NO:2; amino acid residues 2-487 of SEQ ID NO:8; and amino acids 2-496 of SEQ ID NO:4. According to the Examiner, the specification does not enable any person skilled in the art to which it pertains to make and use the invention commensurate in scope with these claims. Applicant respectfully adresses this rejection as follows.

The Examiner is respectfully referred to the Synopsis of Application of Written Description Guidelines. Example 14 entitled "product by function" specifically present a claim referring to an amino acid sequence 95% identical to another amino acid sequence. The circumstances examplified therein are very similar to that of the

present situation. Of course the present invention exemplifies numerous nucleic acid sequences encoding Staufen (e.g. human, mouse, *C. elegans*, and *Drosophila*, the former three being newly presented). In addition, the invention exemplifies a number of biological functions: HIV infectivity, TAR RNA binding, *bicoid* RNA binding, dsRNA binding (e.g. poly(rI)-poly(rC)) and tubulin binding. In addition, the present invention provides alignments of the different Staufen sequences and also characterizes structure-function relationships of Staufen.

In view of the above and foregoing and the ample contemplation of "variants", as stipulated in the Written Description Guidelines: "functional derivatives" (page 29, line 14 to line 11 and page 30); "functional variant" (page 30, lines 15 -17); the "at least 95% identical" language (page 31, lines 18 - 24); "mutation" (page 32, lines 7 - 15); amino acid sequences "at least 95% homologous", "at least 95% identical" (page 33, lines 2 - 5); it should be clear that the specification at least fully "contemplates" variants as taught in Example 14 of the Guidelines.

Thus, the Applicant respectfully submits that isolated nucleic acid sequences 95% identital to the recited Staufen sequences while maintaining the claimed biological functions are clearly enabled.

The nucleic acid sequences of claims 4 and 24 as amended herein, are 95% identical to a nucleic acid encoding a Staufen polypeptide. As stated in the Written Description Guidelines, the procedures for making variants of polypeptides (e.g. Staufen) having 95% identity are conventional in the art (and the specification also teaches some). In addition, as exemplified by the cloning of the mouse, human and *C. elegans* Staufen nucleic acids, a method to identify other protein sequences and nucleic acids encoding same having the claimed functional activities is disclosed (see Examples 7 through 12 of the present application). Moreover, the claimed variants are restricted to variants possessing the specified functional activities (i.e. binding to tubulin, to Tar RNA, to *bicoid* RNA or to poly(rI)-poly(rC) RNA). In addition, Applicant respectfully submits that the species disclosed are representative of the genus because all claimed members have at least 95% structural identity with the

referenced nucleic acid and because of the disclosed and exemplified assays for identifying the at least 95% identical variants of the recited sequence retaining the claimed biological function.

Thus, since the specification clearly teaches how to use the functional Staufen proteins, and since the specification provides sequence alignments (Figures 1 and 1'), and identifies essential functional domains of the polypeptide (e.g. see example 12), Applicant submits that the amended claims are clearly enabled to a person skilled in the art to which the present invention pertains.

The Examiner further objects to claims 4 and 24, alleging that "the specification does not teach conditions under which the recited nucleic acids could bind to the recited ligand" (i.e., "RNA, HIV genomic RNA, or tubulin"). The Examiner thus argues that binding "is not enabled". Applicant respectfully traverses the Examiner's rejection as follows.

Amended claims 4 and 24 now recite the following "ligands": TAR RNA, *bicoid* RNA, poly(rI)-poly(rC) and tubulin. Applicant respectfully submits that the specification teaches specific conditions under which these interactions may be measured. For example:

- Figure 8 shows the interaction between hStau and TAR RNA.
- Figure 3, Examples 4 and 10 disclose RNA binding assays and demonstrate that Staufen binds to *bicoid* and poly(rI)-poly(rC) RNAs.
- Figure 4, Examples 5 and 11 describe tubulin binding assays and demonstrate that Staufen indeed binds to tubulin. Finally,
- Example 12 discloses the mapping of the RNA and tubulin binding domains.

Thus, assays which allow to determine if the claimed nucleic acids can bind to dsRNAs such as TAR RNA, *bicoid* RNA, Poly(rI)-poly(rC); and tubulin are well described in the application.

The Examiner also refers to the instant specification at pages 55-56. More particularly, the Examiner states that "Staufen can bind to any dsRNA or RNA that form secondary structure or RNA/DNA hybrid, which indicates that the binding is specific to any specific RNA substrate". The Examiner further states "the binding properties recited in the claims could not be used for isolating the nucleic acid molecules that would meet the claimed limitations". The Examiner additionally states that "binding to RNA substrate may not be sufficient to isolate polynucleotides that encode a protein that bind a specific RNA". First, Applicant respectfully submits that Staufen is not taught to bind "any" RNA but to highly structured RNA or RNA/DNA hybrids (as well as tubulin). TAR is a specific example of a highly structured, and stable double-stranded RNA sequence. The binding of Staufen to a number of dsRNA is clearly enabled and supported by the instant invention. The current amendments recite such nucleic acid ligands. Second, the Applicant does not claim a method for isolating any sequence which would bind to a dsRNA and then determine its sequence to verify if it is within the 95% identical limitation. Applicant respectfully submits that having determined the sequence of two mammalian Staufen sequences as well as that of *C. elegans*, and having determined functions thereof (e.g. binding to TAR) the person of skill in the art can without undue experimentation identify homologs, variants, alleles of the claimed mammalian Staufen sequences that fall within the identity and functional limitations of the claims.

Applicant respectfully submits that in view of the instant amendement, the combination of the 95% identity to Staufen limitation together with the disclosed and claimed functional activity of Staufen, claims 4 and 24 are clearly enabled. Applicant believes that the above and foregoing also address the note by the Examiner that "the claims are to nucleic acid while the function is being studied of the protein encoded and thus an artisan would require extensive undue experimentation to isolate nucleic acids that would meet the recited functional characteristics" (top of page 4). Applicant re-emphasizes that the pioneering sequences which are claimed depend on a sequence limitation as well as on a limitation to specific and fully enabled biological functions, thus warranting a

protection of sequences having "at least 95% sequence identity" and therefore being by definition Staufen variants.

Applicant acknowledges with thanks the withdrawal of the Written Description rejection of claims 4 and 24 (paragraph 7 of the Office Action). However, Claim 4 remain rejected under 35 U.S.C. 112, **first** paragraph, as failing to comply with the written description requirement. The (j) embodiment (apparently mistakenly described as (i) by the Examiner) of claim 4, recites a sequence which hybridizes under high stringency conditions to certain full length sequences but not to parts of their sequences. According to the Examiner, the "specification does not [sic] disclose any such nucleic acid molecules". In view of the cancellation of the "(j)" embodiment in claim 4, this rejection has been rendered moot.

Finally, claim 4 is rejected under 35 U.S.C. 112, **second** paragraph. The Examiner finds unclear how a nucleic acid sequence could hybridize to the full length sequence but not to part of the sequence (embodiment (j) of claim 4). In view of the cancellation of embodiment (j) of claim 4, applicant respectfully submits that the rejection has also been rendered moot.

In view of the above and foregoing Applicant respectfully requests that the Examiner withdraw all remaining rejections under 35 U.S.C. 112, first and second paragraphs, and allow all pending claims.

CONCLUSIONS

The rejections of the claims are believed to have been overcome by the present amendments and remarks. From the foregoing, Applicants respectfully submit that a Notice of Allowance is believed to be next in order, and such an action is earnestly solicited.

Authorization is hereby given to charge deposit account no. 07-1742 for any deficiencies or overages in connection with this response.

Respectfully submitted,

GOUDREAU GAGE DUBUC

Julie Gauvreau
Reg. No. 52,532

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(514) 397-4374